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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,004	01/05/2001	Anthony P. Shuber	EXT-048	4632

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EXAMINER
CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/755,004	SHUBER, ANTHONY P.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,17-20 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,18-20 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Acknowledgement is made for the request to establish continued prosecution application (RCE) (Paper NO. 17) filed on March 7, 2003. The request for RCE is accepted and is established with the status of the application as follows:

a. the filling date of this RCE is established as 01/05/2001;

b. Claims 1-9, 17-20, and 24 are considered for examination in view of submitted IDS.

2. Information Disclosure Statement (Paper Nos. 16, 18 and 19) filed on 2/27/2003, 3/7/2003 and 3/24/03 respectively, have been entered and considered.

3. These instant claims 1-9, 17-20 and 24 are considered for continued prosecution in view of the IDS submitted.

New issues

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 1-6, 8, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Gramley et al. (J Clin. Microbiol., Vol. 37, No.7, pp. 2236-2240, 1999).

With reference to the instant claim 1, 6, 8, 18, Gramley et al. teach a method for detecting a Helicobacter pylori infection wherein Gramley et al. disclose that the method comprises (a) detecting a Helicobacter nucleic acid (DNA) present in a patient stool sample (see page 2236, column 2, paragraphs 1-2, page 2237, column 1, paragraph 1, column 2, paragraph 1, page 2238,

column 2, paragraph 1, Fig. 3); (b) identifying a patient having indicative of Helicobacter pylori infection if the amount and length of the nucleic acid (DNA) present in the patient (positive signal intensity) exceeds an amount indicative of an absence (negative signal) of the Helicobacter pylori infection (see page 2238, Fig. 3). Fig. 3 of the disclosure of Gramley et al. indicates southern blot hybridization signals wherein the intensity of signals in comparison to positive signals (presence of H.pylori) and negative signals (absence of H.pylori), indicate the comparison of amount of hybridization signals for the presence or absence of H.pylori infection.

With reference to the instant claims 2-5, Gramley et al. teach that the method comprises (i) detecting a high-integrity (intact) Helicobacter pylori nucleic acid present in a patient sample (gastric biopsy specimens and stool samples) (see page 2238, Fig.2 and 3); (ii) comparing an amount of high-integrity Helicobacter pylori nucleic acid present in the patient sample to an amount of a non-Helicobacter pylori nucleic acid (see page 2238, column 1, paragraphs 1-2, column 2, paragraphs 1-2, Fig. 2 and 3). Fig. 2 and 3 of the disclosure of Gramley et al. indicates universal amplifiable DNA- 224 bp PCR product in case of gastric biopsy specimen (Fig.2) and 148 bp PCR product in case of a stool sample (Fig.3) and southern blot hybridization signals for H.pylori specific amplification products (139 bp). The hybridization signals as compared to the amplifiable (non-H.pylori nucleic acid) in Figs. 2 and 3 clearly indicates the presence or absence of H.pylori infection in comparison to the amount of non-H.pylori nucleic acid.

B. Claims 1-6, 8, 18, 20 are rejected under 35 U.S.C. 102(a) as being anticipated by Powell et al. (WO 00/29618).

With reference to the instant claim 1, 6, 8, 18, Powell et al. teach a method for detecting a Helicobacter pylori infection wherein Powell et al. disclose that the method comprises (a)

detecting a Helicobacter nucleic acid (DNA) present in a patient stool sample (see page 8, lines 26-32, page 9, lines 19-25, page 11, lines 1-32, page 12, lines 1-32, page 13, lines 1-2); (b) identifying a patient having indicative of Helicobacter pylori infection if the amount (hybridized product) and length of the nucleic acid (DNA) present in the patient (positive signal intensity) exceeds an amount indicative of an absence (negative signal) of the Helicobacter pylori infection (see page 12, lines 10-21, page 15, lines 20-32, page 17, lines 1-14).

With reference to the instant claims 2-5, Powell et al. teach that the method comprises (i) detecting a high-integrity (intact) Helicobacter pylori nucleic acid present in a patient sample (gastric biopsy specimens and stool samples) (see page 11, lines 1-32, page 12, lines 1-21); (ii) comparing an amount of high-integrity Helicobacter pylori nucleic acid present in the patient sample to an amount of a non-Helicobacter pylori nucleic acid (amplifiable DNA- using universal primers) (see page 11, lines 23-32, page 12, lines 1-8).

With reference to the instant claim 20, Powell et al. also teach that the method comprises determining threshold of H. pylori infection based on the amounts of H. pylori DNA (see page 13, lines 5-12).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 7, 9, 19, and 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gramley et al. (J Clin. Microbiol., Vol. 37, No.7, pp. 2236-2240, 1999) and in view of Lapidus et al. (USPN. 6,143,529).

Gramley et al. teach a method for detecting a Helicobacter pylori infection wherein Gramley et al. disclose that the method comprises (a) detecting a Helicobacter nucleic acid (DNA) present in a patient stool sample (see page 2236, column 2, paragraphs 1-2, page 2237, column 1, paragraph 1, column 2, paragraph 1, page 2238, column 2, paragraph 1, Fig. 3); (b) identifying a patient having indicative of Helicobacter pylori infection if the amount and length of the nucleic acid (DNA) present in the patient (positive signal intensity) exceeds an amount indicative of an absence (negative signal) of the Helicobacter pylori infection (see page 2238, Fig. 3). Fig. 3 of the disclosure of Gramley et al. indicates southern blot hybridization signals wherein the intensity of signals in comparison to positive signals (presence of H.pylori) and negative signals (absence of H.pylori), which indicate the comparison of amount of hybridization signals for the presence or absence of H.pylori infection.

Gramley et al. teach that the method comprises (i) detecting a high-integrity (intact) Helicobacter pylori nucleic acid present in a patient sample (gastric biopsy specimens and stool samples) (see page 2238, Fig.2 and 3); (ii) comparing an amount of high-integrity Helicobacter pylori nucleic acid present in the patient sample to an amount of a non-Helicobacter pylori nucleic acid (see page 2238, column 1, paragraphs 1-2, column 2, paragraphs 1-2, Fig. 2 and 3). Fig. 2 and 3 of the disclosure of Gramley et al. indicates universal amplifiable DNA- 224 bp PCR product in case of gastric biopsy specimen (Fig.2) and 148 bp PCR product in case of a stool sample (Fig.3) and southern blot hybridization signals for H.pylori specific amplification products (139 bp). The hybridization signals as compared to the amplifiable (non-H.pylori nucleic acid) in Figs. 2 and 3 clearly indicates the presence or absence of H.pylori infection in comparison to the amount of non-H.pylori nucleic acid. However, Gramley et al. did not teach

addition of ion chelator (at least 150mM) to the patient sample and immobilized probe hybridization assay.

Lapidus et al. teach a method for improving sensitivity and specificity of obtaining nucleic acids from patient samples wherein Lapidus et al. disclose that the method comprises (i) adding EDTA, an ion chelator to the patient sample, at a concentration preferably at least 150mM (see column 7, lines 28-46); (ii) use of immobilized probe to capture nucleic acid present in a patient sample (see column 10, lines 29-66); (iii) amount of DNA grater than about 200 bp (about includes 150 or 160, or 170 or any number around 200) in length (column 29, lines 42-55); (iv) patient sample comprises bodily excretions (e.g. stool, pus, sputum or saliva) (see column 6, lines 19-23).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of detecting helicobacter pylori nucleic acid as taught by Gramley et al. with the method of adding EDTA as taught by Lapidus et al. because Lapidus et al. states that "use of at least 150mM EDTA greatly improves the yield of nucleic acid from stool sample" (see column 7, lines 40-42). Further, as noted in *In re Aller*, 105 USPQ 233 at 235, More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Routine optimization is not considered inventive and no evidence has been presented that the concentration of buffer selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art. An ordinary practitioner would have

been motivated to combine the method of Gramley et al. with the inclusion of limitations (adding EDTA and use of immobilized probe to capture specific nucleic acids) as taught by Lapidus et al. in order to achieve the expected advantage of a rapid and sensitive method for detecting Helicobacter pylori in clinical samples because inclusion of such limitations would enhance the sensitivity and specificity of the method.

Allowable Subject Matter

5. Claim 17 is allowable.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
May 14, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER